MEDICAL DEVICES COMPRISING IONICALLY AND NON-IONICALLY CROSSLINKED POLYMER HYDROGELS HAVING IMPROVED MECHANICAL PROPERTIES

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to medical devices comprising polymer hydrogels having improved mechanical properties.

2. Description of Related Art

Medical devices adapted for implant into the body to facilitate the flow of bodily fluids, to serve as vascular grafts or for other purposes have been developed. Typically, these devices include stents, catheters or cannulas, plugs, constrictors, tissue or biological encapsulants and the like.

Typically, many of these devices used as implants are made of durable, non-degradable plastic materials such as polyurethanes, polyacrylates, silicone polymers and the like, or more preferably from biodegradable polymers which remain stable in-vivo for a period of time but eventually biodegrade in-vivo into small molecules which are removed by the body by normal elimination in the urine or feces.

Typical of such biodegradable polymers are polyesters, polyanhydrides and polyorthoesters which undergo hydrolytic chain cleavage, as disclosed in U.S. Pat. No. 5,085,629; crosslinked polysaccharide hydrogel polymers as disclosed in EPA 0507604 A-2 and U.S. Pat. No. 5,057,606 and other ionically crosslinked hydrogels as disclosed in U.S. Pat. Nos. 4,941,870, 4,286,341 and 4,878,907.

EPA 0645150 A-1 describes hydrogel medical devices prepared from ionically crosslinked anionic polymers, e.g. polysaccharides such as calcium alginate or ionically crosslinked cationic polymers such as chitosan, cationic guar, cationic starch and polyethylene amine. These devices are adapted for more rapid in-vivo disintegration upon the administration of a chemical trigger material which displaces crosslinking ions.

Hydrogels offer excellent biocompatibility and have been shown to have reduced tendency for inducing thrombosis, encrustation, and inflammation. Unfortunately, the use of hydrogels in biomedical device applications has often been hindered by poor mechanical performance. Although many medical device applications exist where minimal stresses are encountered by the device in-vivo, most applications require that the device survive high stresses during implantation. Hydrogels suffer from low modulus, low yield stress and low strength when compared to non-swollen polymer systems. Lower mechanical properties result from the swollen nature of hydrogels and the non-stress bearing nature of the swelling agent, e.g., aqueous fluids.

Accordingly, there is a need in the art to provide shaped medical devices which not only offer the advantages of polymer hydrogels in terms of biological compatibility, but which also have improved mechanical properties, e.g. improved strength and modulus properties, such that they retain their shape and stiffness during insertion into the body, such as by delivery through an endoscope, and which also can swell and soften inside the body to enhance patient comfort.

SUMMARY OF THE INVENTION

This invention provides a means of boosting the mechanical performance of shaped medical devices comprising polymer hydrogels, such as stents, so that they may be more easily inserted into the body, and at the same time provides a means to soften such devices in-vivo while retaining the structural integrity of the device.

The invention provides a process for improving the mechanical properties and structural integrity of a shaped medical device comprising a crosslinked polymeric hydrogel, said process comprising subjecting an ionically crosslinkable polymer composition to crosslinking conditions such that both ionic and non-ionic crosslinks are formed resulting in a polymeric hydrogel, wherein a medical device of improved structural integrity is obtained upon selective removal of said crosslinking ions from said polymeric hydrogel.

In addition, the invention also provides a process for improving the mechanical properties and structural integrity of a shaped medical device comprising a polymeric hydrogel, said process comprising:

a) providing a crosslinked polymeric hydrogel composition containing a non-ionic crosslink structure, said hydrogel polymer characterized as being ionically crosslinkable and having a primary shape;

b) imparting a secondary shape to said hydrogel polymer composition; and

c) subjecting said hydrogel polymer to ionic crosslinking conditions to ionically crosslink said hydrogel polymer while retaining said secondary shape.

A medical device substantially conforming to the primary shape of said hydrogel is obtained upon selective removal of the crosslinking ions from said crosslinked polymeric hydrogel, such as by removal of said ions after the device is implanted into the body.

The invention also provides a shaped medical device having improved mechanical properties comprising a crosslinked polymeric hydrogel, said hydrogel containing both an ionic and a non-ionic crosslink structure. The device is characterized by improved structural integrity after selective removal of said ionic crosslinking ions as compared with an otherwise identical device containing only an ionic structure.

The invention further provides a medical procedure comprising insertion of the above-described medical device into a human or animal body to form an implant, followed by the selective removal of at least a portion of the crosslinking ions from the implant in-vivo to soften the implant. Where the implant is later surgically removed, it may be once again subjected to ionic crosslinking conditions to ionically re-crosslink the implant prior to removal from the body.

DETAILED DESCRIPTION OF THE INVENTION

The ionically crosslinkable polymers from which the medical devices of this invention may be fabricated may be anionic or cationic in nature and include but are not limited to carboxylic, sulfate, hydroxy and amine functionalized polymers, normally referred to as hydrogels after being crosslinked. The term "hydrogel" indicates a crosslinked, water insoluble, water containing material.

Suitable crosslinkable polymers which may be used in the present invention include but are not limited to one or a mixture of polymers selected from the group consisting of polyhydroxy ethyl methacrylate, polyvinyl alcohol, polyacrylamide, poly (N-vinyl pyrolidone), polyethylene oxide, hydrolysed polyacrylonitrile, polyacrylic acid, polymethacrylic acid, polyethylene amine, alginic acid, pectinic acid, carboxy methyl cellulose, hyaluronic acid, heparin, heparin sulfate, chitosan, carboxymethyl chitosan, chitin,